Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL

INIST-CNRS

Leukaemia Section
Short Communication

i(5)(p10) in hematological malignancies

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Published in Atlas Database: June 2018
Online updated version : http://AtlasGeneticsOncology.org/Anomalies/i05p10ID1825.html
Printable original version : http://documents.irevues.inist.fr/bitstream/handle/2042/70576/06-2018-i05p10ID1825.pdf
DOI: 10.4267/2042/70576

Abstract

Isochromosome of the short arm of chromosome 5 is an infrequent chromosome anomaly that has been reported in myeloid, and less frequently in in lymphoid malignancies, including leukemia and lymphomas.

Keywords

AML, acute monoblastic leukemia, isochromosome 5p, clonal evolution.

Clinics and pathology

Disease

Chronic or acute myeloid malignancies and lymphoid neoplasms.

Note See also i(5)(p10) in acute myeloid leukemia

Epidemiology

Chronic myeloproliferative disorders (MPD) in 8 (4M/4F aged 19 to 81 years; median 66 years): 1 chronic myeloid leukemia (Markovic et al., 2000) and 7 MDS (Christodoulou et al., 2004; Lessard et al., 2007; Herry et al., 2010; Jimenez-Sousa et al., 2010; Douet-Guilbert et al., 2011; Reddi et al., 2012; Giudici et al., 2013).

Acute myeloid leukemia (AML) in 18 (9M/9F aged 8 to 86 years, median 64 years): 2 AML (Flach et al., 2011; Hartmann et al.,2014), 2 acute myeloblastic leukemia without maturation (M1) (Calabrese et al., 2000; Choi et al., 2007), 2 acute myeloblastic leukemia with maturation (M2) (Tamura et al., 1998; Herry et al., 2007), 1 acute promyelocytic leukemia (M3) (Goldschmidt et al., 2010), 2 acute myelomonocytic leukemia (M4) (El-Rifai et al., 1997; Panani 2006), 8 acute monoblastic leukemia (M5) (Yunis 1984; Slovak et al., 1991; Schoch et al 2001; Schmidt et al., 2004; Gervais et al., 2008; Paar et al., 2013) and 1 acute erythroleukemia (M6) (Herry et al., 2010) patient.

Multiple myeloma was diagnosed in a single male (Sawyer et al., 2014).

Lymphoid malignancies in 12 patients. B-cell lymphomas in 7 (3M/4F aged 55, 71, 78 and 86 years, 3 unknown) (Hashimoto et al., 1995; Dierlamm et al., 1997; Wlodarska et al., 1999; Hernandez et al., 2001; Bastard et al., 1992; Cook et al., 2004; Johnson et al., 2008), and there was a 54-years old male with chronic lymphocytic leukemia (Jarosova et al., 2010).

3 patients were diagnosed with T-cell lymphoid malignancies (2M/1F aged 38 and 69 years, 1 unknown) (Heinonen et al., 1994; Lepretre et al., 2000; Nelson et al., 2008) and an 11- years old male with bilineage or biphenotypic leukemia (La Starza et al., 1993).

Etiology

38 patients (20 M/18 F aged 8 to 86 years; median 69 years). Myeloid malignancies mainly (26 patients): 18 AML, 7 MDS and 1 CML.

In 10 of the 18 AML patients the cells were of monoblastic (8 patients)/monocytic (2 patients) lineage.

Among them, 4 had therapy-related MDS, 1 had therapy-related AML (t-MDS/t-AML), and one patient had chronic myelogenous leukemia in myeloid blast phase.

The primary diagnoses for patients with t-MDS/t-AML were mediastinal germ cell tumor (Christodoulou et al., 2004), carcinoma of the ovary (Lessard et al., 2007), breast carcinoma (Gervais et al., 2008) and multiple myeloma (Jimenez-Sousa et al., 2010; Reddi et al., 2012).

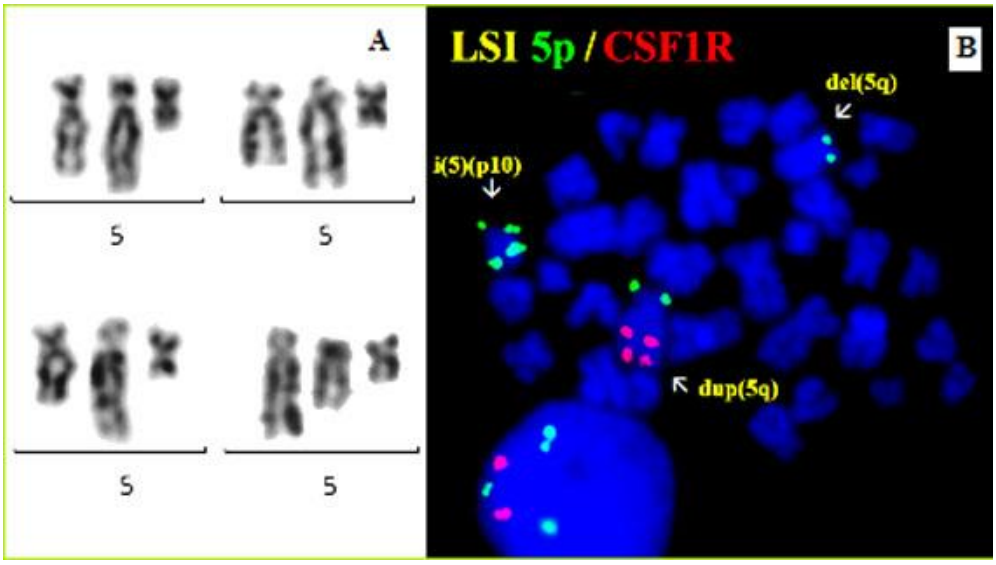

Figure 1. Partial karyotypes with i(5)(p10) (A). Fluorescence in situ hybridization with LSI CSF1R/D5S23, D5S721 probe hybridizing to 5p15.2 and 5q33-34 sequences (Abbott Molecular/Vysis, US) showing combination of chromosome 5 abnormalities: deletion of the long arm of chromosome 5, duplication of 5q33-34 sequences and isochromosome i(5)(p10) (B).

The occurrence of i(5)(p10 was not restricted to myeloid malignancies as it was also detected in 8 patients with B-cell and in 3 with T-cell lymphoid malignancies.

Prognosis

i(5)(p10 is frequently part of complex karyotypes representing clonal evolution that may reflect genomic instability. Most of these patients showed a more aggressive course of the disease and poor response to chemotherapy (Paar et al., 2013).

Genetics

Note

The formation of i(5)(p10) may be observed in two patterns: (1) i(5)(p10) replacing a normal chromosome 5 leading to the loss of the long arm of chromosome 5 and duplication of its short arm. (2) It occurs as a supernumerary +i(5)(p10) chromosome, with two normal copies of chromosome 5, resulting in 5p tetrasomy, that has been reported in AML and B-cell lymphoid malignancies, but not in MDS.

Cytogenetics

Note

Because of their similar cytogenetic appearance, the incidence of i(5)(p10) may be underestimated as it might have been misinterpreted as 5q deletion, a known chromosome abnormality in myeloid malignancies. Therefore, to discriminate between 5q deletion and i(5)(p10), fluorescence in situ hybridization using locus specific probes for 5p/5q sequences is recommended.

Cytogenetics morphological

Presents as i(5)(p10) resulting in 5q deletion in 7 MPD, 6 AML, 1 CLL, 1 mature B-cell neoplasm and 3 T-cell lymphoid malignancies. Among them, sole anomaly in 1 MDS (Douet-Guilbert et al., 2011), sole additional anomaly to +8 in 1 MDS (Jimenez-Sousa et al., 2010), to -Y in 1 MDS (Reddi et al., 2012) and found as +8 and complex karyotypes in 2 AML (El-Rifai et al., 1997; Herry et al., 2007). In 1 MDS patient, 2 copies of isochromosome 5p and a single normal chromosome 5 have been detected (Giudici et al., 2013).Presents as a supernumerary +i(5)(p10) in 11 out of 17 AML, in the bilineage or biphenotypic leukemia, in 1 MM an in 6 out of 7 B-cell lymphomas. Among them, +8 was found in 8 AML patients (Panani 2006; Yunis 1984; Schoch et al 2001; Slovak et al., 1991; Calabrese et al., 2000; Flach et al., 2011) while it was a sole additional anomaly to +8 in 3 patients (Schoch et al 2001; Panani 2006). Found with 14q32 rearrangement and complex karyotypes in 3 out of 6 B-cell lymphomas and as part of complex karyotypes in the remaining patients.

Result of the chromosomal anomaly

Fusion protein

Oncogenesis

Isochromosome of the short arm of chromosome 5 represents a rare but recurrent chromosome anomaly in hematological malignancies.

Its occurrence has been mainly associated with myeloid malignancies, especially AML with

monocytic lineage, but it has also been reported in lymphoid disorders, including leukemia and lymphomas. When present in a single copy, i(5)(p10) results in 5p trisomy and 5q monosomy, that might be similar to a 5q- syndrome. Therefore, loss of material from chromosome 5q arm and gain of 5p material may play a key pathogenic role in these patients. In contrast, when presents as a supernumerary +i(5)(p10) chromosome, the formation of isochromosome leads to 5q disomy and 5p tetrasomy, thus duplication of its short arm leading to copy gain imbalances could contribute to proliferative advantage of the cells. i(5)(p10) is mainly observed as an additional chromosomal abnormality to known anomalies such as trisomy 8 in myeloid malignancies or is part of a complex karyotypes, likely representing a secondary cytogenetic event in the majority of patients.

References

Baker CM. Maximizing mailed questionnaire responses. Image J Nurs Sch. 1985 Fall;17(4):118-21

Calabrese G, Fantasia D, Spadano A, Morizio E, Di Bartolomeo P, Palka G. Karyotype refinement in five patients with acute myeloid leukemia using spectral karyotyping. Haematologica. 2000 Nov;85(11):1219-21

Choi WT, Folsom MR, Azim MF, Meyer C, Kowarz E, Marschalek R, Timchenko NA, Naeem RC, Lee DA. C/EBPbeta suppression by interruption of CUGBP1 resulting from a complex rearrangement of MLL. Cancer Genet Cytogenet. 2007 Sep;177(2):108-14

Christodoulou J, Schoch C, Schnittger S, Haferlach T. Myelodysplastic syndrome (RARS) with +i(12p) abnormality in a patient 10 months after diagnosis and successful treatment of a mediastinal germ cell tumor (MGCT). Ann Hematol. 2004 Jun;83(6):386-9

Douet-Guilbert N, Basinko A, De Braekeleer E, Guéganic N, Bovo C, Le Bris MJ, Morel F, Eveillard JR, Berthou C, Herry A, De Braekeleer M. Isolated 5p isochromosome in myelodysplastic syndrome: report of the first case. Leuk Res. 2011 Nov;35(11):e193-7

El-Rifai W, Elonen E, Larramendy M, Ruutu T, Knuutila S. Chromosomal breakpoints and changes in DNA copy number in refractory acute myeloid leukemia. Leukemia. 1997 Jul;11(7):958-63

Flach J, Dicker F, Schnittger S, Schindela S, Kohlmann A, Haferlach T, Kern W, Haferlach C. An accumulation of cytogenetic and molecular genetic events characterizes the progression from MDS to secondary AML: an analysis of 38 paired samples analyzed by cytogenetics, molecular mutation analysis and SNP microarray profiling. Leukemia. 2011 Apr;25(4):713-8

Goldschmidt N, Yehuda-Gafni O, Abeliovich D, Slyusarevsky E, Rund D. Interstitial insertion of RARα gene into PML gene in a patient with acute promyelocytic leukemia (APL) lacking the classic t(15;17). Hematology. 2010 Oct;15(5):332-7

Herry A, Douet-Guilbert N, Morel F, Le Bris MJ, Guéganic N, Berthou C, De Braekeleer M. Isochromosome 5p and related anomalies: a novel recurrent chromosome abnormality in myeloid disorders. Cancer Genet Cytogenet. 2010 Jul 15;200(2):134-9

Huttmann B. Quit wasting time with "nursing rituals". Nursing. 1985 Oct;15(10):34-9

Jimenez-Sousa MA, Ferro MT, Talavera M, Villalon C, Cabello P, Laraña J, Herrera P, Garcia Sagredo JM. Myelodysplastic syndrome with isochromosome 5p and trisomy 8 after treatment of a multiple myeloma Cancer Genet Cytogenet 2010 Dec;203(2):345-7

Lessard M, Hélias C, Struski S, Perrusson N, Uettwiller F, Mozziconacci MJ, Lafage-Pochitaloff M, Dastugue N, Terré C, Brizard F, Cornillet-Lefebvre P, Mugneret F, Barin C, Herry A, Luquet I, Desangles F, Michaux L, Verellen-Dumoulin C, Perrot C, Van den Akker J, Lespinasse J, Eclache V, Berger R; Groupe Francophone de Cytogénétique Hématologique. Fluorescence in situ hybridization analysis of 110 hematopoietic disorders with chromosome 5 abnormalities: do de novo and therapy-related myelodysplastic syndrome-acute myeloid leukemia actually differ? Cancer Genet Cytogenet 2007 Jul 1;176(1):1-21

Markovic VD, Bouman D, Bayani J, Al-Maghrabi J, Kamel-Reid S, Squire JA. Lack of BCR/ABL reciprocal fusion in variant Philadelphia chromosome translocations: a use of double fusion signal FISH and spectral karyotyping Leukemia 2000 Jun;14(6):1157-60

Panani AD. Gain of an isochromosome 5p: a rare recurrent abnormality in acute myeloid leukemia In Vivo 2006 May-Jun;20(3):359-60

Reddi DM, Lu CM, Fedoriw G, Liu YC, Wang FF, Ely S, Boswell EL, Louissaint A Jr, Arcasoy MO, Goodman BK, Wang E. Myeloid neoplasms secondary to plasma cell myeloma: an intrinsic predisposition or therapy-related phenomenon? A clinicopathologic study of 41 cases and correlation of cytogenetic features with treatment regimens Am J Clin Pathol 2012 Dec;138(6):855-66

Schmidt HH, Strehl S, Thaler D, Strunk D, Sill H, Linkesch W, Jäger U, Sperr W, Greinix HT, König M, Emberger W, Haas OA. RT-PCR and FISH analysis of acute myeloid leukemia with t(8;16)(p11;p13) and chimeric MOZ and CBP transcripts: breakpoint cluster region and clinical implications Leukemia 2004 Jun;18(6):1115-21

Schoch C, Bursch S, Kern W, Schnittger S, Hiddemann W, Haferlach T. Gain of an isochromosome 5p: a new recurrent chromosome abnormality in acute monoblastic leukemia Cancer Genet Cytogenet 2001 May;127(1):85-8

Slovak ML, Nemana L, Traweek ST, Stroh JA. Acute monoblastic leukemia (FAB-M5b) with t(8;14)(p11;q11 1) Cancer Genet Cytogenet

Tamura S, Takemoto Y, Hashimoto-Tamaoki T, Mimura K, Sugahara Y, Senoh J, Furuyama JI, Kakishita E. Cytogenetic analysis of de novo acute myeloid leukemia with trilineage myelodysplasia in comparison with myelodysplastic syndrome evolving to acute myeloid leukemia Int J Oncol 1998 Jun;12(6):1259-62

Yunis JJ. Recurrent chromosomal defects are found in most patients with acute nonlymphocytic leukemia Cancer Genet Cytogenet 1984 Feb;11(2):125-37

This article should be referenced as such:

Zamecnikova A. i(5)(p10) in hematological malignancies. Atlas Genet Cytogenet Oncol Haematol. 2019; 23(10):304-306.